

## Publication

A bufadienolide-enriched fraction of *Bryophyllum pinnatum* effectively inhibits myometrium contractility in vitro

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*Bryophyllum pinnatum* has been used since the 1970s to prevent premature labour, first in anthroposophic hospitals and, more recently, also in the main Swiss perinatal centres. However, it is not known which compounds in *B. pinnatum* leaves contribute to the tocolytic effect. Here we studied the effects of a flavonoid-enriched fraction, the corresponding flavonoid aglycon mixture, a bufadienolide-enriched fraction, and *B. pinnatum* leaf press juice on human myometrial contractility in vitro. The strength (area under the curve and amplitude) and frequency of contractions were recorded using strips of human myometrium mounted in an organ bath system. Cell viability assays were performed with the human myometrium hTERT-C3 and PHM1 – 41 cell lines. Repeated addition of the flavonoid-enriched fraction, flavonoid aglycon mixture, bufadienolide-enriched fraction, or *B. pinnatum* leaf press juice led to a progressive decrease of contraction strength, without jeopardising the vitality of myometrium strips. The bufadienolide-enriched fraction was the most active, since 1 µg/mL of the bufadienolide-enriched fraction lowered the area under the curve to  $40.1 \pm 11.8\%$  of the initial value, whereas 150 µg/mL of the flavonoid-enriched fraction, 6.2 µg/mL of the flavonoid aglycon mixture, and 10 µg/mL of the *B. pinnatum* leaf press juice were required to achieve comparable inhibition. A progressive increase of contraction frequency was observed, except in the case of the flavonoid aglycon mixture, which did not affect frequency. None of the test substances decreased myometrial cell viability, even at concentrations of 500 µg/mL of the flavonoid-enriched fraction, 40 µg/mL of the flavonoid aglycon mixture, 3.8 µg/mL of the bufadienolide-enriched fraction, and 75 µg/mL of the *B. pinnatum* leaf press juice, i.e., higher than those used in the myometrium experiments. Given the concentrations of flavonoids in the flavonoid-enriched fraction and *B. pinnatum* leaf press juice, and of bufadienolides in the bufadienolide-enriched fraction and *B. pinnatum* leaf press juice, it appears that bufadienolides may be mainly responsible for the relaxant effect.

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